REMARKS

Applicants have reviewed the Office Action mailed on June 3, 2004 and offer the following remarks. Reconsideration and allowance of the pending claims in view of the above amendments and the following remarks is respectfully requested.

Rejection under 35 USC §101 and §112, 1st paragraph:

On page 2 of the Office Action, the Examiner has rejected claims 4, 8, 9, 13 and 24-29 under 35 U.S.C.§101 and §112, 1st paragraph. In summary, the Examiner has stated that the claimed isolated nucleic acid molecules lack a specific and substantial asserted utility or a well-established utility and, consequently, one skilled in the art would not know how to use the claimed invention.

The Examiner states that "[w]hile the specification asserts that the polypeptide of SEQ ID NO: 2 is a protein related to the UDP-glucuronosyltransferase family of proteins and it appears that the closest structural homologs are UDP-glucuronosyltransferases, the claimed invention lacks utility" for the following reasons set forth by the Examiner: (1) the specification fails to provide substrates for the polypeptide of SEQ ID NO: 2, or (2) the specification fails to provide any information as to which type of UDP-glucuronosyltransferase that SEQ ID NO: 2 belongs. The Examiner cited Jin *et al.* (*Biochem. Biophys. Res. Commun.* 194(1):496-503, 1993) as providing support for her assertions that UDP-glucuronosyltransferases are separated into two families based on their evolutionary divergence. The Examiner further asserts that the type of compounds glucuronidated is dependent upon the family of the UDP-glucuronosyltransferase.

Further, the examiner stated that in view of the substrates or the family to which the UDP-glucuronosyltransferase belongs, the asserted utility "is not substantial since it will require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use.."

Applicants respectfully traverse this rejection based on the following remarks.

In answer to the Examiner's concerns regarding the identification of the family to which the UDP-glucuronosyltransferase belongs, the polypeptide of SEQ ID NO:2, shows homology to the specific subfamily 2 within the UDP-glucuronosyltransferase

superfamily, as evidenced by the homologous nucleotides XP_003547, NP_006789, NP_001068, JN0619, AAC95002, NP_001067, and so forth, as listed in Figure 1, page 2 of 2. Proteins of the UDP-glucuronosyltransferase family of enzymes, such as the polypeptide of SEQ ID NO:2, have specific functions and utilities that are asserted in the specification and well established in the art. On pages 7 and 8 of the Specification as originally filed, and in Jin *et al.* (*Biochem. Biophys. Res. Commun., Ibid*), the UDP-glucuronosyltransferase subfamily is involved in metabolism of various drugs, and carcinogens. References that support the Applicant's assertions of utility were disclosed on page 8, last paragraph. Jin *et al.* discussed the substrates that class 1 and class 2 family members of the UDP-glucuronosyltransferase family utilize. These and other references establish a utility and thus, enablement for the invention.

Thus, since other members of the UDP-glucuronosyltransferase family of enzymes are known to metabolize the substances listed on page 8 of the specification, and in the references cited therein, one of skill in the art would reasonably expect the polypeptide of SEQ ID NO:2 to also metabolize these and similar substances, and therefore to be specifically useful and commercially valuable for treating, diagnosing, and/or prognosing various disclosed diseases and conditions, such as a target for inhibition in cancer chemotherapeutic regimen, for example (see page 8, first paragraph). Consequently, one of skill in the art would recognize that the claimed invention does have "real world" uses, such as to act as a target to aid in prevention of cancer caused by xenobiotic carcinogens, for example. The HepG-2 cells, disclosed on page 9 of the specification, in Figure 1 and in Jin *et al.,* are well-known cell line in the art for determining metabolism of various compounds.

Thus, the specification does provide an enabling written description of the polypeptide of SEQ ID NO:2. Undue experimentation would not be required by one of skill in the art to use the claimed invention in light of the guidance presented, the state of the art in the area of UDP-glucuronosyltransferase enzymes, the skill of those in the art, and so forth (these factors are set forth in *In re Forman* and cited by the Federal Circuit in *In re Wands*).

Therefore, the claimed invention is supported by both specific and substantial utilities and, consequently, one of ordinary skill in the art would know how to use the claimed invention.

In contrast to the Examiner's assertions, the claimed isolated nucleic acid molecules, such as SEQ ID NOS:1 and 3, that encode a specified amino acid sequence, SEQ ID NO:2, and methods of making and using such nucleic acid molecules have several uses that meet the requirements of 35 U.S.C.§101 and the first paragraph of 35 U.S.C.§112. These, as well as the accepted state of the art, view that such molecules have uses within the commercial marketplace in the drug development cycle, since they encode previously unidentified members of important pharmaceutical targets, and therefore, establishes the utility of the claimed invention.

The U.S. Patent and Trademark Office Utility Guidelines set forth the utility requirement that a claimed invention must have a specific, substantial and credible utility. These requirements are defined in broad terms in cases such as *Brenner v. Manson,* 148 USPQ 689 (S. Ct. 1966) and in the recently adopted Utility Guidelines from the USPTO.

The Examiner stated that the present invention failed to disclose any properties of the present invention, SEQ ID NO: 2 that associated with any disease state. However, such a requirement substantially conflicts with the decision made by the CCPA.

The CCPA in *Nelson v. Bowler*, 206 USPQ 881 (CCPA 1980), clearly accepted a showing of less than a specific therapeutic use of a claimed chemical compound as satisfying the utility requirement.

> *The CCPA held that where a claim does not provide evidence of pharmacological activity of a claimed compound, although it does not establish a specific therapeutic use, manifests a practical utility because knowledge of pharmacological activity is beneficial to the public in that it makes faster and easier for medical researchers to combat illnesses. Nelson v. Bowler, 206 USPQ 881 (CCPA 1980).*

The notion that a recognized valuable addition to even entry points of the drug discovery cycle advances the art sufficient to establish a "usefulness" of a claimed invention should not be ignored. Similar to the *Nelson* case, the present invention, which is drawn to isolated nucleic acid molecules that encode a UDP-glucuronosyltransferase (SEQ ID NO: 2), has useful value in the drug discovery process even though the molecule may not be associated with a specific treatment and/or diagnosis of a particular

disease. According to *Nelson*, the present invention provides sufficient knowledge and information that is beneficial to the public, and provides sufficient guidance for researchers to use the claimed subject matter to develop disease treatments and/or diagnostics. It is well recognized that UDP-glucuronosyltransferase are important targets for drug action. The public disclosure of a new member of this family through the patenting process clearly advances the art and augments the capabilities of biomedical researchers to combat illnesses.

The utility rejection raised by the Examiner also conflicts with the case *Juicy Whip v. Orange Bang* (Fed. Cir. 1999). *Juicy Whip* held that, in order to violate the utility requirement, an invention must be "totally incapable of achieving a useful result." The polypeptides and encoding nucleic acid molecules of the present invention are well known in the art to be valuable drug targets and therefore have readily apparent commercial utilities, such as for screening potential drug compounds, producing antibodies, developing hybridization probes and primers, etc. In addition to the uses disclosed in the specification and discussed herein for the polynucleotides of the present invention, other utilities are readily apparent to one of ordinary skill in the art based on the observed tissue specific expression patterns. Thus, for example, the proteins/nucleic acids of the present invention are commercially useful for developing therapeutic agents for treating diseases affecting these tissues. Therefore, the present invention is not "totally incapable of achieving a useful result." Instead, it is useful.

The specification and figures show that the protein of the present invention has a high homology to the UDP-glucuronosyltransferase family. Figure 1, page 2 of 2 demonstrates a high homology with a human UDP-glucuronosyltransferase . Therefore, the Applicants have provided more than a broad class of proteins; Applicants have provided the identification of a specific protein and a nucleic acid encoding said protein, and thus there is a specific and credible utility of the claimed invention. As such, there is also an enablement for one of skill in the art to make and use the invention.

Thus, the disclosure of the function of the UDP-glucuronosyltransferase family is sufficient. Such a function is quite specific for UDP-glucuronosyltransferase proteins and differentiates them from other proteins. As such, this function is specific enough to

define a use for novel UDP-glucuronosyltransferase proteins and UDP-glucuronosyltransferase-encoding nucleic acid molecules in the drug discovery process.

Novel UDP-glucuronosyltransferase proteins/nucleic acids are commercially useful for developing therapeutics/diagnostics for these and other pathologies. Thus, there is overwhelming evidence in the art to support the utility of novel UDP-glucuronosyltransferase proteins and encoding nucleic acid molecules. Not all nucleic acid molecules, and actually a very limited number, of the 3 billion bases that make up the human genome will encode a protein for these and the other disclosed uses. These uses are quite specific for the UDP-glucuronosyltransferase family of proteins, even though each member may play a somewhat different role in cellular responses and pathologies. Even though each member may have a somewhat different role in biology and disease, each is a specific composition of matter having substantial, specific and credible uses that the vast majority of other isolated nucleic acid molecules do not possess.

By placing a new member of the UDP-glucuronosyltransferase protein family into the public domain through the patenting process, the present invention is not only a clear advancement over the prior art (a newly discovered protein/gene) but also enables significant advancement in medicine and further discovery. The Utility requirement cannot be used to contradict the reasons for the patent system, to encourage early disclosures of inventions so that others can benefit from, improve upon, and further develop such inventions. This is particularly important in medicine, wherein early disclosure of key inventions (such as new UDP-glucuronosyltransferase proteins and encoding nucleic acid molecules) is needed to facilitate the early development of new therapies and diagnostics to treat illnesses.

The grant of a patent to the claimed isolated nucleic acid molecule and the resultant disclosure of the nucleic acid and protein sequences to the public will certainly shorten the process for medical researchers to discover other novel uses for the present UDP-glucuronosyltransferase-encoding nucleic acids. One example disclosed in the specification is that the present nucleic acid molecules can be used to produce protein targets for identifying agents that bind to the protein targets and modulate protein function. Such agents can be used to precisely determine which biological and

pathological processes the protein is involved in. All of this later discovery and refinement will be done using the presently claimed material. These uses are clearly commercial and substantial uses that are specific for a very limited number of proteins/nucleic acid molecules.

In addition to serving as targets for developing molecular probes and therapeutic agents, the disclosed uses of the claimed nucleic acid molecules as probes, primers, and chemical intermediates, particularly in biological assays, is sufficient to satisfy the requirements of 35 USC §101 and §112. The claimed invention is directed to nucleic acid sequences that encode a UDP-glucuronosyltransferase with a specified amino acid sequence (SEQ ID NO: 2), such as SEQ ID NOS:1 and 3. Exemplary uses of the nucleic acid sequences are clearly recited in the specification. Among the examples, the nucleic acid molecules are useful as hybridization probes for messenger RNA molecules, transcript/cDNA molecules, genomic DNA, and variants thereof. An expression vector comprising the nucleic acid sequences can be made that expresses the UDP-glucuronosyltransferase protein. Such uses are specific for the claimed nucleic acid molecules, and the products of such uses will be clearly different (and hence specific for the claimed molecules) than what would be produced using a different nucleic acid molecule for the same purpose.

In view of law and fact, the Utility standard interpreted by the USPTO guidelines is too high. The disclosure of activity of the expressed polynucleotide is not required by any statute or case law interpreting the utility requirement of Section 101, and the enablement requirement of Section 112, first paragraph. The commercial value of a gene that encodes a previously unidentified member of the UDP-glucuronosyltransferase family, members of which are well known in the art to be commercially valuable drug targets, is sufficient to satisfy the utility and enablement requirements. Therefore, Applicants respectfully request that the Examiner withdraw the rejection.

Rejection Under 35 U.S.C. §102(e)

The Examiner has rejected claims 4, 8, 9, 24 and 27-30 under 35 U.S.C. §102(e) as being anticipated by Policky *et al.,* (U.S. Patent Application No. 2004/0029125 (Serial Number 10/258,080) and WO 01/79468). The Examiner states that the priority of the '125 and '468 publications has been claimed to U.S. Provisional Application No. 60/197,590, filed on April 13, 2000. The Examiner additionally stated that "[i]t has been determined that the polypeptide of SEQ ID NO: 2 and the polynucleotide of SEQ ID NO: 11" in the Policky et al. published documents were first disclosed in the provisional application.

The Applicants respectfully traverse the rejection. The Examiner did not provide the Applicants with factual evidence to support her assertions, such as a copy of the provisional application, and in fact provided an alignment that only disclosed a translation and alignment (polynucleotide to amino acid sequence alignment) referring only to the later filed 2004/0029125 application. As supporting evidence was not provided by the Examiner, the Applicants assert that the rejection is improper, given that the present application claims priority to Provisional Application No. 60/228,893, filed on August 30, 2000, which is prior to the April 12, 2001 filing date of the '125 application by Policky *et al.,* and thus is not available as prior art under 35 U.S.C. §102(e).

However, the Applicants will address the rejection to answer the concerns of the Examiner. The Applicants respectfully direct the attention of the Examiner to SEQ ID NOs: 1 and 11 of the '125 application. While the Examiner provided a translation alignment of SEQ ID NO: 11 of the '125 application, she did not provide a nucleic acid to nucleic acid alignment. There is no factual evidence provided by the Examiner that ANY of the nucleic acids of the '125 application are "completely complementary" to SEQ ID NO: 1 as required in claim 30 of the present application, or "consist" of SEQ ID NO: 1 of the present application, as required in claim 4(b).

As the reference does not teach each and every limitation of the claim, *i.e.,* a nucleic acid of SEQ ID NO: 1, the rejection is improper and must be withdrawn.

Note by Examiner:

The Examiner has also noted U.S. Publication No. 2004/0029221 (Baker *et al.*; Serial No. 10/206,915) which the Examiner asserts as disclosing SEQ ID NOs: 521 and 522, and which claims priority to U.S. Provisional Application 60/209,832, filed June 5, 2000. The Examiner stated that

> At this time, priority claim to provisional application 60/209832 has not been verified. If it is later verified that SEQ ID NO: 521-522 were first disclosed in provisional application 60/209832, claims 4, 8-9, 24, 27-30 will be rejected under 35 U.S.C. 102(e) as being anticipated by Baker et al. This will not be considered as new ground(s) of rejection.

The Applicants note the Examiner's assertions that U.S. Publication No. 2004/0029221 (Baker *et al.*; Serial No. 10/206,915) discloses SEQ ID NO: 522 and a polynucleotide (SEQ ID NO: 521) encoding the polypeptide of SEQ ID NO: 522. The Examiner asserts that SEQ ID NO: 521 is 100% identical to SEQ ID NO: 2 of the present application.

The Applicants respectfully traverse the assertions of the Examiner. Additionally, the Applicants respectfully direct the Examiner to the provisions of MPEP §706.07 which sets forth the conditions under which a reference may be applied as a new grounds for rejection and when an action may be made final. As the Examiner has not rejected any claims as being anticipated by the '221 publication, any subsequent rejection of claims over the '221 application will constitute a new grounds for rejection and thus, the subsequent action cannot be made final. The MPEP §706.07 further states that the subject matter of the claims must be thoroughly searched and considered prior to making a rejection. As the Examiner admitted that the grounds for her concerns have not been established, *i.e.,* the claim to priority to the 60/209,832 have not been verified, then the claims have not been thoroughly searched and thus a rejection cannot have been made in the present Office Action.

Assuming *in arguendo*, that the claims are determined by the U.S.P.T.O. to have been properly rejected over Baker *et al.* in the present Office Action, which they have not, the Applicants offer the following arguments to preserve their rights. The following arguments in no manner are an admission by the Applicants that a rejection has been made. The following arguments are made to address the issues raised by the Examiner only, and do not constitute a response to a rejection.

The Examiner did not provide the Applicants with factual evidence to support her assertions, such as a copy of the provisional application, and in fact provided an alignment that only disclosed a translation and alignment (polynucleotide to amino acid sequence alignment) referring only to the later filed 2004/0029221 application (Serial Number 10/206,915). As supporting evidence was not provided by the Examiner, the Applicants assert that given that the present application claims priority to Provisional Application No. 60/228,893, filed on August 30, 2000, which is prior to the June 6, 2001 filing date of the '915 application by Baker *et al.*, the '915 application would not available as prior art for any possible future rejections under 35 U.S.C. §102(e). While the Examiner provided a translation alignment of SEQ ID NO: 521 of the '915 application, she did not provide a nucleic acid to nucleic acid alignment. There is no factual evidence provided by the Examiner that ANY of the nucleic acids of the '915 application are "completely complementary" to SEQ ID NO: 1 as required in claim 30 of the present application, or "consist" of SEQ ID NO: 1 of the present application, as required in claim 4(b).

Conclusion

Claims 4, 8, 9, 13 and 24-30 are currently pending. In view of the above remarks, Applicants respectfully submit that the application and claims are in condition for allowance, and request that the Examiner reconsider and withdraw all outstanding rejections. If for any reason the Examiner finds the application other than in condition for allowance, the Examiner is invited to call the undersigned agent should the Examiner believe a telephone interview would advance prosecution of the application.

Applicants respectfully assert that the claims are in condition for allowance.

Respectfully submitted,

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